## Remarks

Claims 8, 10, 24 and 27 have been amended. Claim 25 has been cancelled without prejudice or disclaimer. New claims 31-37 have been added. Claims 8, 10-12 and 23-24, 27 and 29-37 are pending.

Claims 8 and 24 have been amended for the sake of improved clarity. Claims 10 and 27 have been amended for consistency with the amendments made to claim 8.

New claims 31-37 have been added to further protect the invention of the present application. New claim 31 is derived from previously pending claim 24. New claims 32-33 are based on claims 29-30.

New claims 34-36 specify that the recited blood substitute interferent is cross-linked hemoglobin. Support for claims 34-36 is provided at page 14, lines 8-13.

New claim 37 is supported by the specification as originally filed.

Support for the amendments made to claims 8 and 24 is provided at page 14, line 8 to page 15, line 8; page 18, line 1 to page 20, line 23, and page 23, line 1 to page 24, line 6 of the specification.

Applicant further incorporates all prior responses by reference to preserve all issues for appeal.

### *Claim Rejections–35 USC 103*

The Office Action rejects claims 8, 10-12 and 23-30 under 35 U.S.C. 103(a) as being unpatentable over Davis in view of Sagusa, Gimpel, Simon and Christenson, Leissing or Mullins.

More particularly, the Office Action alleges that it would have been obvious to one of ordinary skill in the art at the time the invention was made to include substances such as blood substitutes disclosed by Christenson, Leissing or Mullins as interfereing substances into the correction method of Davis. Applicant respectfully traverses Examiner's rejection.

Davis discloses a method of estimating a change in an analyte in a whole-blood sample, which is due to the hemolysis of red blood cells, comprising separating a plasma fraction from the whole blood sample, estimating the quantity of extracellular hemoglobin in the plasma fraction, estimating a change in the analyte concentration in the sample due to the hemolysis of whole blood cells, and adjusting the apparent concentration of the analyte to account for the proportion of same which is due to the hemolysis of red blood cells (column 6, lines 3-16; column 8, lines 40-56).

Davis suggests that the amount of hemoglobin in the plasma sample may be determined by measuring the reflectance of the sample using a wavelength at which hemoglobin exhibits a maximum absorbance, and by using a graph of reflectance vs. hemoglobin concentration, derived from a set of samples containing known amounts of hemoglobin, to determine the concentration of hemoglobin in the plasma sample (column 8, lines 18-21 and 28-36). Davis, however, does not particularly teach or suggest a method for determining the concentration of an analyte in a specimen comprising a blood substitute interferent, as defined in present claim 8. In particular, Davis does not specifically teach or suggest a method of determining a corrected concentration of an analyte, which involves the use of a calibration algorithm for a blood substitute interferent, **and** a calibration algorithm for a non-blood substitute interferent, which were developed using a calibration set comprising variable amounts of the blood substitute interferent and the non-blood substitute interferent. In addition, Davis does not specifically teach or suggest a method as defined in present claim 24 and new claim 31, which involves the use of a calibration algorithm

developed using a calibration set comprising variable amounts of hemoglobin and cross-linked hemoglobin to determine a value of hemoglobin or cross-linked hemoglobin.

Christenson et al. disclose that hemoglobin based blood substitutes interfere with routine chemical tests, and the dilution of the sample is suggested as a way to avoid interference. There is no teaching or suggestion in Christenson et al., as to how an interferent may be identified and/or quantified in a blood sample comprising a blood substitute. Applicant, therefore, submits that Christenson et al. help define the problem in the art that the present invention is solving, that being, determining the concentration of an interferent in a sample, and if desired, correcting for the concentration of the interferent when establishing the concentration of an analyte in the sample.

Applicant submits that Christenson does not cure the defects in Davis as a documents that precludes patentability of the pending claims.

Leissing et al. disclose modifications of clinical chemistry methods to overcome interferences from diaspirin crosslinked haemoglobin (DCLHb). The abstract teaches that filtering samples through an Amicon Centrifree micropartition system can remove concentrations of DCLHb up to 5000 mg/dl, producing a filtrate with molecular weight constituents less than 30000 daltons. Furthermore, for the detection of some analytes, dilution of the sample is required, in a method similar to that disclosed in Christenson. Leissing et al. do not teach or suggest the subject matter that is disclosed by the claims of the instant application. Leissing, as noted for Christenson, define the problem in the art that the present invention is solving.

Mullins et al. teaches that fluosol may lead to potential errors in the analysis of blood specimens. There is no disclosure or suggestion as to how an interferent may be identified and/or quantified in a blood sample that comprises a blood substitute.

Rather, Mullins et al. further define the problem that the present invention is addressed to solving.

As Davis does not specifically teach or suggest that its method could be used with samples containing blood substitute interferents, such as those disclosed in Christenson et al., Leissing et al., or Mullins et al., one skilled in the art would not, therefore, be motivated to combine the teachings of Davis with Christenson et al., Leissing et al., or Mullins et al. to arrive at the method of claims 8, 10-12 or 23-30 of the present application.

The Office Action further alleges that it would have been obvious to one of ordinary skill in the art at the time the invention was made to use different wavelengths as taught in Sagusa to differentiate between true hemolysis and plasma discoloration due to circulating colored substances as taught by Simon in the Davis method. Applicant respectfully disagrees.

The Sagusa patent teaches a colorimetric method for measuring components in a sample in the presence of interfering chromogens. In the method disclosed in the Sagusa patent, a color former is added to blood samples for colouring, and measurements for specific components are determined based on the light absorbance caused by the colouring. The measurements for specific components are corrected by the degree of chyle, degree of hemolysis and degree of icterus, which are determined at different wavelengths.

Simon et al., teaches that iron dextran therapy may cause a red-brown discolouration of the plasma simulating a hemolytic transfusion reaction. The method used in Simon et al. to detect the iron, comprises adding Gomori's iron stain (page 342, last paragraph, left hand column) and obtaining a blue colour.

There is no teaching or suggestion in Sagusa or Simon et al. of a method of determining the concentration of an analyte contained in a specimen using the method as defined in claim 8 or 24 or new claim 31 of the present application, as no exogenous reagent is added to the sample in the methods defined in the claims of the present application. It is, therefore, respectfully asserted that even if the calibration algorithms of claims 8 and 24, as well as new claim 31, are construed as being algorithms developed using analyses of absorbance or reflectance over a plurality of wavelengths, the methods defined by the present claims do not involve a step of converting an analyte to a chromophore, as required by the method of Sagusa or Simon et al. Furthermore, neither Sagusa nor Simon et al. disclose a correction method using a calibration algorithm developed using a calibration set including a blood substitute interferent, and a non-blood substitute interferent, such as hemoglobin. One skilled in the art would not, therefore, be motivated to combine the teaching of Sagusa and Simon et al. with that of Davis, and one, or more of Christenson et al., Leissing et al. or Mullins et al. to arrive at the presently claimed invention.

The Office Action further alleges that it would have been obvious to one of ordinary skill in the art at the time the invention was made to use a derivative spectroscopic method as shown by Gimpel for correction in the Davis method. Applicant respectfully disagrees.

Gimpel et al., discloses a method of measuring total bilirubin concentrations in cerebrospinal fluid by using derivative spectroscopy and the formation of azobilirubin derivatives. Gimpel et al. Does not, however, provide any teaching or suggestion of a method for determining the concentration of bilirubin without using azobilirubin derivatives.

It is respectfully asserted that even if the calibration algorithms of claims 8 and 24 are construed as being algorithms developed using derivative analyses of spectra, the

methods defined by the present claims do not involve a step of converting an analyte to a chromophore, as required by the method of Gimpel et al. One skilled in the art would not, therefore, be motivated to combine the teaching of Gimpel et al. with that of Davis, and one, or more of Christenson et al., Leissing et al. or Mullins et al. to arrive at the presently claimed invention.

Applicant, therefore, submits that Davis, in combination with of Christenson et al., Leissing et al. or Mullins et al., and any of the other cited references do not teach or suggest the method of determining the concentration of an analyte in a specimen containing a blood substitute interferent, as claimed in claims 8 and 10-12, 23 and 25-30. Furthermore, Applicant respectfully submits that Davis in combination with Christenson, Leissing or Mullins, or any of the other cited references, do not teach or suggest the method of determining the presence of true hemolysis, as claimed in claim 24, or pseudohemolysis, as claimed in new claim 31.

Referring now to the specific language in claim 8, wherein it recites, in part, providing a first calibration algorithm for said blood substitute interferent, a second calibration algorithm for a non-blood substitute interferent, a first linear equation defining a relationship between a measured concentration of said analyte and a concentration of said blood substitute interferent. Applicant can not find where any of the applied documents (Davis, Sagusa, Gimpel, Simon Christenson, Leissing and Mullins) teach or suggest first and second calibration algorithms and first linear equations as recited in claim 8. Applicant requests allowance of claim 8 as the applied documents due not teach all of the features of claim 8.

If the rejection of claim 8 is maintained in the next office action, applicant request that the examiner specifically point to passages in either Davis, Sagusa, Gimpel, Simon Christenson, Leissing or Mullins where the claim 8 features of first and second calibration algorithms and first linear equations as recited in claim 8 are taught to clarify issues for appeal.

Referring now to the specific language in claim 24, wherein it recites, in part, measuring an absorbance of radiation of said specimen, wherein said measuring is performed in the absence of any reaction step that generates a chromophore within said specimen, and incorporating said absorbance measured in step (i) into a calibration algorithm developed using a calibration set comprising variable amounts of hemoglobin and a blood substitute interferent to determine a value of hemoglobin. Applicant can not find where any of the applied documents (Davis, Sagusa, Gimpel, Simon Christenson, Leissing and Mullins) teach or suggest first and second calibration algorithms and first linear equations as recited in claim 24. Applicant requests allowance of claim 24 as the applied documents due not teach all of the features of claim 24.

If the rejection of claim 24 is maintained in the next office action, applicant request that the examiner specifically point to passages in either Davis, Sagusa, Gimpel, Simon Christenson, Leissing or Mullins where the claim 24 features of first and second calibration algorithms and first linear equations as recited in claim 24 are taught to clarify issues for appeal.

In determining validity of a patent claim, it is not enough to show that each of the components of the claim was known and had been used in other similar systems. Guided by the defendants, the court below treated each reference as teaching one or more of the specific components for use in the patented system, although the patented system did not then exist. Thus, the court reconstructed the patented system, using the blueprint of the patent claims. This is legal error. *Interconnect Planning Corp. v. Feil,* 774 F.2d 1132 (Fed. Cir. 1985). Applicant submits that the Office Action violates the above case law set forth by the Federal Circuit. The Office Action merely selects components, which are in the present claims, from the applied documents using the present claims as a blueprint. Reconsideration and withdrawal of the

rejections based on Davis, Sagusa, Gimpel, Simon Christenson, Leissing and Mullins are respectfully requested.

The Examiner has the burden under 35 U.S.C. ' 103 to establish a prima facie case of obviousness. In re Fine, 837 F.2d 1071, 1074, 5 U.S.P.Q.2d (BNA) 1596, 1598 (Fed. Cir. 1988). In combining prior art references to construct a prima facie case, the Examiner must show some objective teaching in the prior art or some knowledge generally available to one of ordinary skill in the art that would lead an individual to combine the relevant teaching of the references. Id. The M.P.E.P. contains explicit direction to the Examiner that agrees with the In re Fine court:

> In order for the Examiner to establish a prima facie case of obviousness, three base criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. M.P.E.P. §2142 (citing In re Vaeck, 947 F.2d 488, 20 U.S.P.Q.2d (BNA) 1438 (Fed. Cir. 1991)).

The fact that the references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. In re Mills, 16 USPQ2d 1430 (Fed. Cir. 1990); M.P.E.P. §2143.01. That is, unless all three of the conditions described in M.P.E.P. §2142 are met, a prima facie case of obviousness is not established, and rejection under 35 U.S.C. §103 is improper.

Applicant submits that the applied documents do not teach all of the features of the claims. Applicant further submits that there is no suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Applicant further submits that there is no reasonable expectation of success in combining the applied documents. That is, it appears that the Office Action is improperly relying on an obvious-to-try standard, which has been regularly rejected by the courts.

Examiner is respectfully requested to withdraw the rejection to claims 8, 10-12 and 23-30 under Section 35 U.S.C. § 103(a).

## CONCLUSION

Applicant respectfully submits that the claims are in condition for allowance and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney at (612) 349-9587 to facilitate prosecution of this application. If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,
JAMES SAMSOONDAR ET AL.
By their Representatives,
SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
P.O. Box 2938
Minneapolis, MN 55402
(612) 349-9587

Date 13 Feb '04

By _____
Timothy B Clise
Reg. No. 40,957

CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 13thday of February, 2004.

PATRICIA A. HULTMAN

Name

Signature